Pyridine Derivatives of Nimesulide as New Promising Anti-inflammatory Agents

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N-(3-phenylamino-4-pyridinyl)trifluoromethanesulphonamide or FJ29 is a pyridine analogue of nimesulide, a COX-2 preferential inhibitor that was withdrawn from market because of liver toxicity. Compound FJ29 showed *in vitro* higher cyclooxygenases (COXs) inhibitory potency than nimesulide as well as an important anti-inflammatory activity *in vivo*. However, this compound expressed a rather low COX-2 (type 2 cyclooxygenase) selectivity ratio. So, we realised the synthesis of new pyridine derivatives of nimesulide while keeping the *N*-(3-phenylamino-4-pyridinyl)sulphonamide scaffold in order to obtain original compounds exhibiting a potent COXs inhibitory activity with a COX-2 preferential profile. The COXs inhibitory potency of synthesized compounds was evaluated on a human whole blood model while the anti-inflammatory activity was determined in a rat lambda carrageenan-induced pleurisy model. Drug plasmatic concentration obtained at the end of the in vivo experiments was determined by means of a SPE-LC (Solid Phase Extraction – Liquid Chromatography) method. Various experimentations allowed us to identify compounds exhibiting a strong COXs inhibitory activity *in vitro* with an important anti-inflammatory potency *in vivo*. Plasmatic assays also showed a different pharmacokinetic profile between nimesulide and its pyridine analogues.